Roundup causes non-alcoholic fatty liver disease at very low doses

Cutting-edge molecular profiling analyses reveal that the popular weedkiller Roundup causes liver damage at doses permitted by regulators. Report: Claire Robinson

The weedkiller Roundup causes non-alcoholic fatty liver disease at very low doses permitted by regulators worldwide, a new peer-reviewed study shows. The study is the first ever to show a causative link between consumption of Roundup at a real-world environmentally relevant dose and a serious disease.

The new peer-reviewed study, led by Dr Michael Antoniou at King's College London, used cutting-edge profiling methods to describe the molecular composition of the livers of female rats fed an extremely low dose of Roundup weedkiller, which is based on the chemical glyphosate, over a 2-year period.

The dose of glyphosate from the Roundup administered was thousands of times below what is permitted by regulators worldwide.

The study revealed that these animals suffered from non-alcoholic fatty liver disease (NAFLD).

Dr Antoniou said: “The findings of our study are very worrying as they demonstrate for the first time a causative link between an environmentally relevant level of Roundup consumption over the long-term and a serious disease – namely non-alcoholic fatty liver disease.

“Our results also suggest that regulators should reconsider the safety evaluation of glyphosate-based herbicides.”

Potentially serious implications for human health

The new results demonstrate that long-term consumption of an ultra-low dose of Roundup at a glyphosate daily intake level of only 4 nanograms per kilogram of bodyweight per day, which is 75,000 times below EU and 437,500 below US permitted levels, results in NAFLD.

Regulators worldwide accept toxicity studies in rats as indicators of human

NAFLD currently affects 25% of the US population and similar numbers of Europeans. Risk factors include being overweight or obese, having diabetes, or having high cholesterol or high triglycerides (a constituent of body fat) in the blood. However, some people develop NAFLD even if they do not have any of these known risk factors. The new study raises the question of whether exposure to Roundup is a hitherto unrecognized risk factor.

Symptoms of NAFLD include fatigue, weakness, weight loss, loss of appetite, nausea, abdominal pain, spider-like blood vessels, yellowing of the skin and eyes (jaundice), itching, fluid build-up and swelling of the legs and abdomen, and mental confusion.

NAFLD can progress to the more serious condition, non-alcoholic steatohepatitis (NASH). NASH causes the liver to swell and become damaged.

Most people with NASH are between the ages of 40 and 60 years. It is more common in women than in men. NASH is one of the leading causes of cirrhosis in adults in the United States. Up to 25% of adults with NASH may have cirrhosis.

Background to the study

The rat body tissues used in this analysis were obtained from a previous study led by Prof Gilles-Eric Séralini of the University of Caen, France. In this original investigation, rats were given an extremely low, environmentally relevant dose of a commercial Roundup formulation at 0.1ppb (parts per billion)/50ppt (parts per trillion) glyphosate via drinking water for 2 years. Daily intake of glyphosate from the Roundup was 4 nanograms per kilogram of body weight per day, which is thousands of times below what is permitted by regulators.

Analysis of the organs and blood/urine biochemical levels in the original study by Prof Séralini suggested a higher incidence of liver and kidney damage in the animals given Roundup compared to controls given plain drinking water.

Dr Antoniou's group has conducted distinct followup investigations on the rat body tissues from this ultra-low-dose Roundup treatment group, using in-depth molecular analytical procedures and statistical analytical methods that are appropriate for this type of research.

In the first followup investigation, a transcriptomics (gene function profile) analysis was performed on the livers and kidneys from the female animals. The results strongly supported the observations made at an anatomical (organ) and blood/urine biochemical level in the Séralini study – namely that the organs of the animals given Roundup suffered more structural and functional damage than the controls.

(scarring), necrosis (areas of dead tissue), phospholipidosis (disturbed fat metabolism) and damage to mitochondria (the centres of respiration in cells) in the Roundup-fed animals.

However, although transcriptomics analysis is able to predict health or disease status of an organ, it does not provide definitive proof of harm. This is mainly because it does not give a direct measure of the actual biochemistry of the organ under study. Also, alterations in gene function resulting from a test do not always result in the types of changes in physical composition that could lead to disease.

Definitive confirmation of liver disease from low dose of Roundup

In the new study the researchers undertook a followup protein composition profile ("proteomics") and small molecule metabolite biochemical profile ("metabolomics") investigation of the same liver samples to confirm the prediction of disease suggested by the transcriptomics gene expression profile analysis. As the proteomics and metabolomics directly measure the actual composition of the organ, these analytical methods provide a definitive assessment of its health or disease status.

Overall, metabolomics and proteomics disturbances showed a substantial overlap with biochemical hallmarks of NAFLD and its progression to steatohepatosis (serious fatty liver disease). Therefore they definitively confirm that serious liver disease has resulted from chronic ultra-low dose Roundup exposure.

The findings in detail

Proteins significantly disturbed (214 out of 1906 detected), as shown by the proteomics profiling, reflected a type of cell damage from reactive oxygen (peroxisomal proliferation), steatosis (serious fatty liver disease) and necrosis (areas of dead tissue).

The metabolomics analysis (55 metabolites altered out of 673 detected) confirmed lipotoxic (excess fatty tissue) conditions and oxidative stress. Metabolite alterations were also associated with hallmarks of serious liver toxicity.

The new study

Mesnage R, Renney G, Séralini GE, Ward M, Antoniou MN. Multiomics reveal non-alcoholic fatty liver disease in rats following chronic exposure to an ultra-low dose of Roundup herbicide. Scientific Reports, 2016; 6:39328. http://www.nature.com/articles/srep39328

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